PATENT
078061-31851

#8
JRP
4/10/03

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Patent Application of: Morton J. Seligman			: Art Unit	: 1616
Serial No.	:	10/061,025	: Examiner	: M. Haghighatian
Filed	:	January 30, 2000		
Title	:	COMPOSITIONS AND METHODS FOR TREATING ALLERGIC FUNGAL SINUSITIS		

Assistant Commissioner for Patents
Washington, D.C. 20231

DECLARATION UNDER 37 C.F.R. §1.132 OF DR. MORTON J. SELIGMAN

I, Dr. Morton J. Seligman, a citizen and resident of the United States, hereby declare that:

I am the Morton J. Seligman who is the Applicant of the above-captioned Application;

In June 1958, I received a B.A. from Rutgers University, New Brunswick, New Jersey;

In June 1962, I received a M.D. from Albany Medical College of Union University, Albany, New York;

In April 1969, I was certified as a Fellow in the American Academy of Pediatrics.

In November of 1972, I was certified as a Diplomate of the American Board of Allergy and Immunology

In 1973 I was certified as a Fellow of the American Academy of Asthma, Allergy and Immunology

Attached as Exhibit A is my *Curriculum Vitae* setting forth my qualifications as an allergist in the field of Allergic Medicine.

I am familiar with the prosecution including the office action dated December 18th in the captioned Application which office action cites U.S. Patent Application Publication 2002/0061281-A1 - Osbakken et al. (the Osbakken Patent Publication) as a reference.

I am familiar with the Osbakken Patent Publication which discloses the administration of various pharmaceutical agents through an extranasal cloud mist by means of aerosol nebulizer whereas the invention disclosed in the captioned application is directed to administration of montelukast and/or pranlukast for treating allergic fungal sinusitis by intranasal administration such as through a nose spray .

The Osbakken Patent Publication discloses many different pharmaceutical agents which can be administered through an extranasal cloud mist by means of aerosol nebulizer including, in paragraphs [0188] and [0189], montelukast formulated at a dosage of 3.5 ml in 3 milliliters of sterile water.

The Osbakken Patent Publication in paragraphs [006] through [009] discloses Infectious Fungal Sinusitis and its possible treatment which is a different disease than Allergic Fungal Sinusitis which is the disease treated in accordance with the invention of the captioned application.

This Declaration is being submitted to demonstrate that:

a) montelukast administered through an extranasal cloud mist by means of aerosol nebulizer in accordance with the procedure of Osbakken does not provide intranasal delivery of any measurable dose of montelukasts whereas the delivery of montelukasts by an nasal spray in accordance with the invention of the captioned applications provides such intranasal administration; and

b) Allergic Fungal Sinusitis is a different disease from Infectious Fungal Sinusitis since both diseases are caused by different means and have different symptoms.

In order to demonstrate the above with regard to nebulized administration in accordance with the procedure of the Osbakken Patent Publication and intranasal delivery in accordance with the captioned application, the following experiments were performed under my direction and control.

Experimental

Example 1

Osbakken Aerosol administration

A 3.5mg does of monolukast tagged with red ferric oxide was formulated in 3 ml of sterile water. In preparing this dose, the tagged monolukast was ground as a fine powder with a special Cooper mortar and pestle. The fine powder was weighed out on a digital scale. This formulated dose in liquid form was placed in a 6 ml medication chamber of a nebulizer, for aerosolized delivery in accordance with the disclosure in the Osbakken Patent Publication. The nebulizer used was a Medi-Mist nebulizer containing a compressor providing a pressure of 12 psi to drive the liquid forward in a cloud mist. Hooded absorbent filter paper was used as the target receptor. Absorbent filter paper is far more absorbent than the human nose. The nebulizer was fitted in the manner of the Osbakken type nebulizer with a dual nasal adapters and held about 4 cm beneath the hooded absorbent paper. After the contents of the nebulizer were ejected by means of the compressor, the filter paper was examined to determine if red color tagged montelukast was present on the absorbent filter paper.

Example 2

The procedure of Example 1 was repeated except that separate, different dosage formulations were prepared utilizing 0.5 mg and 1.00 mg of montelukast in the nebulizer.. Each of these nasal spray preparations were sprayed on to filter paper in the manner of

Example 1 and examined to determine this red color tagged montelukast was present on the absorbent filter paper

Example 3

Nasal Spray

A 1.0 mg dose of monolukast tagged with red ferric oxide was formulated in 1 ml of saline solution. This formulated dose placed in a typical polyethylene nasal spray container. The nasal spray container was placed about 4.0 cm below hooded absorbent filter paper in the manner of Example 1 of the captioned application. After 10 actuations of the nasal spray 0.1 mg was ejected by mean of squeezing, the nasal spray polyethylene container. The filter paper was examined to determine if red colored monolukast was present on the absorbent filter paper. Complete execution was achieved in about two seconds.

Example 4

The procedure of Example 3 was repeated except that a dosage formulation was prepared utilizing 0.24 mg of monolukast in the nasal spray. This nasal spray preparation was sprayed on to filter paper in the manner of Example 3 and examined to determine this red color tagged montelukast was present on the absorbent filter paper.

Results

Exhibit 2 which is attached hereto sets forth a copy of the photographs of the filter papers produced utilizing 1.0 mg of the nebulized montelukast applied by means of the Osbakken nebulizer versus 1.00 mg dose of montelukast applied to the filter paper by means of a nasal spray as disclosed in the captioned Seligman application. The results of the staining of the filter paper with regard to the 1.00 mg dose utilizing the Osbakken nebulizer was compared to the staining of the filter paper utilizing the 1.00 mg montelukast dose applied by the nasal spray as disclosed in the captioned Seligman application.

Exhibit 3 which is attached hereto sets forth a copy of photograph of the filter papers produced utilizing 0.5 mg of the nebulized montelukast applied by means of the Osbakken

nebulizer versus 0.24 mg dose of montelukast applied to the filter paper by means of the Seligman dose.

The results with regard the 3.5 mg dose of montelukast applied to the filter paper by the nebulizer in accordance with the Osbakken method are not shown. However there was no detectable color on the filter paper. When this result with a 3.5 mg dose applied by the Osbakken method was compared to a lower dose of a0.24 mg dose of montelukast applied by means of a nose spray in accordance with the disclosure in the captioned Seligman application the contrast, while not shown, was the same as that shown in Exhibit 3.

Discussion of Results

As seen from the results in Exhibits 2, 3 and with the 3.5 mg dose applied by the method of Osbakken, dosages of 0.5 mg, 1.00 mg and 3.5 mg, applied by the Osbakken aerosol spray did not deliver any detectable montelukast to the absorbent filter paper. On the other hand, when montelukast is applied to the absorbent filter paper even at lower dosages than that set forth by Osbakken by means of the nasal spray, montelukast is visibly delivered to the absorbent paper. The use of an absorbent filter paper is a means for demonstrating the portion, if any, of the test ingredient that would be administered intranasally into the nose of a human patient. That the active ingredient, which in this case is montelukas,t is deposited on the filter paper demonstrates that the method disclosed in the captioned Seligman application will administer montelukast intranasally to a human patient and that little or no montelukast was deposited on the filter by Osbakken's aerosol nebulizer demonstrates that the method disclosed by Osbakken will not provide an intranasal delivery of montelukast dosage to a human patient.

Allergic Fungal Sinusitis

Paragraph [008] of the Osbakken Patent Publication in discussing the disease specifies an Infectious Fungal Sinusitis not Allergic Fungal Sinusitis . This disease that the Osbakken Patent Publication described is a fungal infection caused by a fungal infection

which can occur in patients with healthy immune systems and not a fungal allergic reaction caused by elevated IgE antibodies in patients who have allergic hypersensitivity

Attached hereto as Exhibit 4 is an article from Dolan, William K., *Journal of Allergy and Clinical Immunology*, **91(1)** January 1993 and attached as Exhibit 5 is an article from Marple, Bradley F., *The Laryngoscope,* **111:**1006-1013 June 2001. As seen from these articles, Infectious Fungal Sinusitis and Allergic Fungal Sinusitis are two different diseases having different diagnostic criteria and treatment options. The differences between Infectious Fungal Sinusitis and Allergic Fungal Sinusitis are described in paragraph 1 on page 1 of the Dolan article and column 1, page 1007 of the Marple et al. article . These articles demonstrate that Infectious Fungal Sinusitis in contrast to Allergic Fungal Sinusitis is invasive whereas Allergic Fungal Sinusitis is caused by an allergic reaction to multiple inhalant allergens and fungi which are different from the fungal strains producing Invasive Fungal Sinusitis. In addition these articles show that treatment of each of these diseases is different.

Conclusions

As seen from the foregoing Dolan and Marple references, Infectious Fungal Sinusitis is a different disease than Allergic Fungal Sinusitis, each disease having different clinical presentations and requiring different treatments.

Therefore, the fact that one treatment may be effective for treating Infectious Fungal Sinusitis does not mean that this treatment would be effective for treating Allergic Fungal Sinusitis.

The results of the aforementioned experiments demonstrate that montelukast is administered intranasally by utilizing a nasal spray in accordance with the invention disclosed in the captioned application.

The results of the aforementioned experiments demonstrate that little or no montelukast is administered intranasally through an extranasal cloud mist by means of aerosol nebulizer in accordance with the method of the Osbakken Patent Publication.

That I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 101 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dr. Morton J. Seligman

Dated: 3/24/03